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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,219	11/17/2003	Manesh Dixit	141-269	4442

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EXAMINER	
SHEIKH, HUMERA N	
ART UNIT	**PAPER NUMBER**
1615	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/715,219	DIXIT ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *15, 17 and 23-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16 and 18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/28/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response to Restriction/Election requirement and Applicant's Arguments/Remarks filed 05/08/07 and the Information Disclosure Statement (IDS) filed 01/28/04 is acknowledged.

Applicant's election with traverse of Group I (claims 1-22) and Applicant's election of species of polymeric binder of (a) cellulose esters/ethers; hydroxypropylmethyl cellulose; hydroxypropyl cellulose in the reply filed on 05/08/07 is acknowledged. The traversal is on the ground(s) that "All claims in Group I and Group II require a mixture of immediate release pellets and extended release pellets. The immediate release pellets in both Group I and Group II require an inert starting seed, a binder and the drug. The extended release pellets in both Group I and Group II require a core and a coating. The core of the extended release pellets comprises/consists essentially of a inert starting seed, a binder and drug and the coating of the extended release pellets comprises/consists essentially of a water-insoluble polymer." This is not found persuasive because, as stated in the Restriction requirement, each of the distinct groups imparts a varied rate of release based on the delivery mechanism via a core or coating degradation. Since each group can impart distinct rates of release, the extended rates of release of each group are capable of supporting a separate patent within the art, based on their respective distinct structures. Thus, each group would have different issues with regards to patentability, enablement and written description. The different groups would also require different searches

in both patent- and non-patent databases and there is no expectation that the searches would be coextensive in scope. This creates an undue burden upon the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 15, 17 and 23-32 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/08/07.

Clams 1-32 are pending in this action. Claims 1, 4, 5, and 16 have been amended. Claims 15, 17, 23-32 have been withdrawn (non-elected invention). Claims 1-14, 16 and 18-22 are rejected.

Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

* * * * *

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9-14, 16 and 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Sherman *et al.* (U.S. Pat. No. 6,274,171).

Sherman *et al.* ('171) disclose a 24 hour extended release dosage formulation of venlafaxine hydrochloride, an antidepressant, which provides better control of blood plasma levels than conventional tablet formulations. The extended release formulation comprises a therapeutically effective amount of venlafaxine hydrochloride in spheroids comprised of venlafaxine hydrochloride, microcrystalline cellulose and optionally, hydroxypropylmethyl cellulose (HPMC) coated with a mixture of ethyl cellulose and hydroxypropylmethyl cellulose (see Abstract); (col. 2, line 63 – col. 3, line 5). A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period, comprising orally administering an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours is also disclosed (see claims 20-25).

The extended release (ER) formulation is an encapsulated formulation that contains venlafaxine hydrochloride as the active drug component, which provides in a single dose, a therapeutic blood serum level over a twenty-four hour period (col. 1, line 11 – col. 2, line 45).

The extended release formulations are those wherein the spheroids are comprised of from about 6% to about 40% venlafaxine hydrochloride by weight, about 50% to about 95% microcrystalline cellulose, by weight and optionally from about 0.25% to about 1% by weight of hydroxypropylmethyl cellulose and coated with from about 2% to about 12% of total weight of film coating comprised of from about 80% to about 90% by weight of film coating of ethyl cellulose and from about 10% to about 20% by weight of film coating of hydroxypropylmethyl cellulose (col. 3, lines 6-40).

The extended release formulations are comprised of venlafaxine hydrochloride in admixture with microcrystalline cellulose and hydroxypropylmethyl cellulose. Formed as beads or spheroids, the drug containing formulation is coated with a mixture of ethyl cellulose and HPMC to provide the desired level of coating, generally from about two to about twelve percent on an wt/wt basis of final product (col. 4, lines 9-67).

Numerous spheroid formulations were prepared using different grades of microcrystalline cellulose and HPMC, different ratios of venlafaxine hydrochloride and filler, different binders such as polvinylpyrrolidone (PVP), methylcellulose, water and polyethylene glycol of different molecular ranges in order to find a formulation that would provide a suitable granulation mix which could be extruded properly. Addition of HPMC 2208 to the venlafaxine hydrochloride-microcrystalline cellulose mix made production of spheroids practical (col. 5, lines 1-22). The resulting spheroids can be coated and tested for their distribution profile. If the dissolution occurs too rapidly, additional coating may be applied until the spheroids present a desired dissolution rate (col. 5, lines 23-32).

The Examples and Table 1 present various venlafaxine hydrochloride formulations and accepted coated spheroid dissolution rates. For instance, Table 1 provides the twenty-four hour therapeutic blood levels for the drug component of the extended release capsules of the invention. Table 1 acceptable coated spheroid dissolution rates are as follows:

Time (hours)	Average % Venlafaxine HCL Released
2	<30
4	30-55
8	55-80
12	65-90
24	>80

These dissolution rates meet the dissolution rates instantly claimed, particularly of instant claims 18-19.

Sherman *et al.* anticipates the instant claims.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-14, 16 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman *et al.* (U.S. Pat. No. 6,274,171) in view of Jerussi *et al.* (U.S. Pat. No. 6,342,533).

Sherman *et al.* ('171), as delineated above, teach a 24 hour extended release dosage formulation of venlafaxine hydrochloride, an antidepressant, which provides better control of blood plasma levels than conventional tablet formulations. The extended release formulation comprises a therapeutically effective amount of venlafaxine hydrochloride in spheroids comprised of venlafaxine hydrochloride, microcrystalline cellulose and optionally, hydroxypropylmethyl cellulose (HPMC) coated with a mixture of ethyl cellulose and hydroxypropylmethyl cellulose (see Abstract); (col. 2, line 63 – col. 3, line 5). A method for providing a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period, comprising orally administering an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from about four to about eight hours is also disclosed (see claims 20-25).

The extended release (ER) formulation is an encapsulated formulation that contains venlafaxine hydrochloride as the active drug component, which provides in a single dose, a therapeutic blood serum level over a twenty-four hour period (col. 1, line 11 – col. 2, line 45).

The extended release formulations are those wherein the spheroids are comprised of from about 6% to about 40% venlafaxine hydrochloride by weight, about 50% to about 95% microcrystalline cellulose, by weight and optionally from about 0.25% to about 1% by weight of hydroxypropylmethyl cellulose and coated with from about 2% to about 12% of total weight of film coating comprised of from about 80% to about 90% by weight of film coating of ethyl cellulose and from about 10% to about 20% by weight of film coating of hydroxypropylmethyl cellulose (col. 3, lines 6-40).

The extended release formulations are comprised of venlafaxine hydrochloride in admixture with microcrystalline cellulose and hydroxypropylmethyl cellulose. Formed as beads or spheroids, the drug containing formulation is coated with a mixture of ethyl cellulose and HPMC to provide the desired level of coating, generally from about two to about twelve percent on an wt/wt basis of final product (col. 4, lines 9-67).

Numerous spheroid formulations were prepared using different grades of microcrystalline cellulose and HPMC, different ratios of venlafaxine hydrochloride and filler, different binders such as polvinylpyrrolidone (PVP), methylcellulose, water and polyethylene glycol of different molecular ranges in order to find a formulation that would provide a suitable granulation mix which could be extruded properly. Addition of HPMC 2208 to the venlafaxine hydrochloride-microcrystalline cellulose mix made production of spheroids practical (col. 5, lines 1-22). The resulting spheroids can be coated and tested for their distribution profile. If the dissolution

occurs too rapidly, additional coating may be applied until the spheroids present a desired dissolution rate (col. 5, lines 23-32).

The Examples at columns 5-10 and Tables present various venlafaxine hydrochloride formulations in extended release capsule forms and their accepted coated spheroid dissolution rates. For instance, Table 1 provides the twenty-four hour therapeutic blood levels for the drug component of the extended release capsules of the invention. Table 1 acceptable coated spheroid dissolution rates are as follows:

Time (hours)	Average % Venlafaxine HCL Released
2	<30
4	30-55
8	55-80
12	65-90
24	>80

These dissolution rates meet the dissolution rates instantly claimed, particularly of instant claims 18-19.

Additionally, as noted above, Sherman *et al.* provides a therapeutic blood plasma concentration of venlafaxine over a twenty-four hour period, comprising orally administering an encapsulated, extended release formulation that provides a peak blood plasma level of venlafaxine in from *about four to about eight hours* (see claims 20-25). The "*about four hours*" explicitly taught by Sherman *et al.* includes the range of "*less than four hours*" claimed herein by Applicant.

While Sherman *et al.* do not explicitly teach all the instant amounts and/or ranges of active ingredient, binder, inert pellet and plasticizer, it is the position of the Examiner that suitable amounts and/or ranges could be determined by one of ordinary skill in the art through the use of routine or manipulative experimentation to obtain the best possible results, as these are variable parameters attainable within the art.

Moreover, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Sherman *et al.* do not teach inclusion of a surfactant and anti-sticking agent.

Jerussi *et al.* ('533) teach oral compositions comprising venlafaxine derivatives and methods for preparing thereof (see Abstract). The compositions provide slow or controlled release of active ingredients (venlafaxine) and can include surface-active agents (i.e., sodium lauryl sulfate), antiadherent agents (i.e., talc), binders, lubricants and the like. The binder/filler is typically present in about 50 to about 99 wt. percent of the composition (see col. 18, lines 8-17); (col. 19, lines 37-45); (col. 20, lines 4-20).

The dosage forms can be in the form of tablets or capsules (col. 16, lines 31-56). The formulations also include starches, sugars, microcrystalline cellulose, HPMC, ethyl cellulose and the like. The dosage forms include multilayered coatings (col. 16, line 57 – col. 17, line 60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the surfactants and anti-sticking agents of Jerussi *et al.* within the venlafaxine compositions of Sherman *et al.* One of ordinary skill in the art would do so because Jerussi *et al.* teach the inclusion of surfactants, such as sodium lauryl surface, useful for its effective wetting properties and also teach antiadherents/fillers such as talc, which aids in avoiding adherence of particles. The expected result would be an enhanced venlafaxine formulation that is beneficial for treating an array of anxiety disorders.

Thus, given the teachings of the prior art discussed above, the instant invention, when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

August 02, 2007

HUMERA N SHEIKH
PRIMARY EXAMINER

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